AMENDMENTS TO THE CLAIMS

This listing of the claims will replace all prior versions and listings of the claims in this application.

LISTING OF THE CLAIMS:

1-56 (Canceled).

57 (Withdrawn and previously presented): A method for loading active agents into liposomes comprising:

a) providing a liposome comprising a gel-phase lipid bilayer and a liposome interior defined by the gel-phase lipid bilayer, said gel phase lipid bilayer comprising phospholipid, wherein said gel-phase lipid bilayer is present below its phase transition temperature; and

b) exposing the gel-phase lipid bilayer to an active agent such that said active agent passes into and through the gel-phase lipid bilayer to load the liposome interior with the active agent.

58 (Canceled).

59 (Withdrawn and previously presented): A method according to claim 57 wherein the liposome is present in a surrounding liquid medium, and wherein the pH of the surrounding liquid medium is greater that the pH of the interior of the liposome to facilitate loading of the active agent.

60 (Withdrawn and previously presented): A method according to claim 57 wherein the lipid bilayer further comprises a surface active agent.

61 (Withdrawn and previously presented): A method according to claim 60 wherein the surface active agent is selected from the group consisting of myristoyl surfactants, palmitoyl surfactants, stearoyl surfactants, polyethylene glycol-derivatized surfactants, glyceryl monopalmitate, glyceryl monooleate, ceramides, PEG-ceramides, polyethylene glycol-polyethylene copolymers, c-i 8 ether linked lysophospatidyl choline, and mixtures thereof

62 (Withdrawn and previously presented): A method according to claim 60 wherein the surface active agent is lysolipid.

63 (Withdrawn and previously presented): A method according to claim 62 wherein the lysolipid is selected from the group consisting of monopalmitoylphosphatidylcholine (MPPC), monolaurylphosphatidylcholine (MLPC), monomyristoylphosphatidylcholine (MMPC), monostearoylphosphatidylcholine (MSPC), and mixtures thereof.

64 (Withdrawn and previously presented): A method according to claim 60, wherein said phospholipid is dipalmitoylphosphatidylcholine (DPPC) and said surface active agent is lysolipid which is monopalmitoylphosphatidylcholine (MPPC).

65 (Canceled).

66 (Currently amended): A liposome, comprising: an active agent and a liposome interior defined by a gel-phase bilayer membrane, wherein the gel-phase bilayer has a phase transition temperature of 39 to 45°C, and wherein the gel-phase lipid bilayer membrane comprises:

(a) a first component which is one or more phospholipids selected from the group consisting of phosphatidyl cholines, phosphatidyl glycerols, phosphatidyl inositols, phosphatidyl ethanolamines, and sphingomyelins, wherein one or more phospholipids have two acyl groups; and

(b) a second component selected from:

(i) one or more surface active agents selected from the group consisting of lysolipids, bile acids, ~~myristoyl surfactants, palmitoyl surfactants, stearoyl surfactants,~~ glyceryl monooleate, ceramides, PEG-ceramides, ~~C18-ether linked lysophosphatidyl choline, polyethylene glycolpolyethylene copolymers,~~ fatty acids, and mixtures thereof; or

(ii) the active agent, wherein the active agent is selected from the group consisting of a pharmacologically active agent, a flavor agent, or a diagnostic agent, or a nutritional agent; and,

(c) wherein the active agent, if absent from the gel-phase lipid bilayer membrane, is present in the liposome interior; and

(d) wherein the amount of the second component in the gel-phase lipid bilayer membrane is sufficient to increase a first percentage of active agent released from the liposome at the phase transition temperature, compared to a second percentage of active agent released in the absence of the second component.

67 (Previously presented): The liposome according to claim 66, wherein the second component is the active agent.

68 (Previously presented): The liposome according to claim 67, wherein the active agent is a pharmacologically active agent selected from the group consisting of ceramides and platelet activating factor.

69 (Previously presented): The liposome according to claim 66, wherein the active agent is within the liposome interior.

70 (Currently amended): A method of administering an active agent to a preselected target site in a subject's body, comprising:

(a) administering a liposome to the subject, wherein the liposome comprises a gel-phase lipid bilayer membrane having a phase transition temperature and a liposome interior defined by the gel-phase bilayer, and an active agent,

wherein the gel-phase lipid bilayer membrane comprises:

(i) a first component which is one or more phospholipids selected from the group consisting of phosphatidyl cholines, phosphatidyl glycerols, phosphatidyl inositols, phosphatidyl ethanolamines, and sphingomyelins, wherein the one or more phospholipids have two acyl groups; and

(ii) a second component selected from:

(I) one or more surface active agents selected from the group consisting of lysolipids, bile acids, ~~myristoyl surfactants, palmitoyl surfactants, stearoyl surfactants,~~ glyceryl monooleate, ceramides, PEG-ceramides, ~~C18-ether linked lysophosphatidyl choline, polyethylene glycol-polyethylene copolymers,~~ fatty acids, and mixtures thereof; or

(II) the active agent, wherein the active agent is selected from the group consisting of a pharmacologically active agent, a flavor agent, or a diagnostic agent, or a nutritional agent; and,

(iii) wherein the active agent, if absent from the gel-phase lipid bilayer membrane is present in the liposome interior; and

(iv) wherein the amount of the second component in the gel-phase lipid bilayer membrane is sufficient to increase a first percentage of active agent released from the liposome at the phase transition temperature, compared to a second percentage of active agent released in the absence of the second component; and

(b) heating the subject's preselected target site to a temperature of about 39°C to 45°C

to release the active agent from the liposome at the target site.

71 (Previously presented): The method of claim 70, wherein the preselected target site comprises tumor tissue.

72 (Withdrawn and previously presented): The method of claim 70, wherein the second component is the active agent.

73 (Previously presented): The method of claim 70, wherein the liposome comprises from about 1 to about 50 mole percent of the second component.

74 (Previously presented): The method of claim 73, wherein the liposome comprises from about 1 to about 30 mole percent of the second component.

75 (Withdrawn and previously presented): The method of claim 72, wherein the active agent is selected from the group consisting of apoptopic agents and platelet activating factor.

76 (Previously presented): The method according to claim 63, wherein the surface active agent is monostearoylphosphatidylcholine (MSPC).

77 (Previously presented): The liposome according to claim 67, wherein the active agent is within the liposome interior and in the gel-phase lipid bilayer membrane.

78 (Previously presented): The method of claim 72, wherein the active agent is within the liposome interior and in the gel-phase lipid bilayer membrane.

79 (Previously presented): The method of claim 57, wherein the liposome interior is loaded with a therapeutic dose of the active agent.

80 (Previously presented): The method of claim 79, wherein the liposome interior is loaded with about 0.01M to about 10M active agent.

81 (Previously presented): The method of claim 80, wherein the liposome interior is loaded with about 0.05M to about 5M active agent.

82 (Previously presented): The method of claim 81, wherein the liposome interior is loaded with about 0.05M to about 5M doxorubicin.

83 (Previously presented): The liposome of claim 66, wherein said second component is one or more bile acids.

84-86 (Canceled).

87 (Withdrawn and previously presented): The liposome of claim 66, wherein said second component is glyceryl monooleate.

88 (Withdrawn and previously presented): The liposome of claim 66, wherein said second component is one or more ceramides.

89 (Withdrawn and previously presented): The liposome of claim 66, wherein said second component is one or more PEG-ceramides.

90-91 (Canceled).

92 (Withdrawn and previously presented): The liposome of claim 66, wherein said second component is one or more fatty acids.

93 (Currently amended): A liposome, comprising: an active agent and a liposome interior defined by a gel-phase bilayer membrane, wherein the gel-phase bilayer has a phase transition region having an onset temperature, a peak transition temperature and an end point temperature, and wherein the gel-phase lipid bilayer membrane comprises:

(a) a first component which is one or more phospholipids selected from the group consisting of phosphatidyl cholines, phosphatidyl glycerols, phosphatidyl inositols, phosphatidyl ethanolamines, and sphingomyelins, wherein one or more phospholipids have two acyl groups; and

(b) a second component selected from:

(i) one or more surface active agents selected from the group consisting of ~~dichain phospholipids~~, lysolipids, bile acids, glyceryl monooleate, ~~myristoyl surfactants, palmitoyl surfactants, stearoyl surfactants,;~~ ceramides, PEG-ceramides, ~~PEG-phosholipids, C18-ether linked lysophosphatidyl choline, block copolymers~~, fatty acids, and mixtures thereof; or

(ii) the active agent, wherein the active agent is selected from the group consisting of a pharmacologically active agent, a flavor agent, or a diagnostic agent, or a nutritional agent; and,

(c) wherein the active agent, if absent from the gel-phase lipid bilayer membrane, is present in the liposome interior; and

(d) wherein the amount of the second component in the gel-phase lipid bilayer membrane is sufficient to increase a first percentage of active agent released from the liposome at the phase transition region, compared to a second percentage of active agent released at the transition region of a liposome comprising only the first component.

94-96 (Canceled).

97 (Previously presented): The liposome of claim 93, wherein said second component is one or more lysolipids.

98 (Previously presented): The liposome of claim 97, wherein said lysolipid is selected from the group consisting of monopalmitoylphosphatidylcholine (MPPC), monolauryl-phosphatidylcholine (MLPC), monomyristoylphosphatidylcholine (MIMPC), monostearoyl-phosphatidylcholine (MSPC), and mixtures thereof

99 (Previously presented): The liposome of claim 98, wherein said lysolipid is monopalmitoylphosphatidylcholine (MPPC).

100 (Previously presented): The liposome of claim 98, wherein said lysolipid is monostearoylphosphatidylcholine (MSPC).

101 (Previously presented): The liposome of claim 98, wherein said lysolipid is monopalmitoylphosphatidylcholine (MPPC) and said first component is dipalmitoylphosphatidylcholine (DPPC).

102 (Previously presented): The liposome of claim 98, wherein said lysolipid is monostearoylphosphatidylcholine (MSPC) and said first component is dipalmitoylphosphatidylcholine (DPPC).

103 (Previously presented): The liposome of claim 102, wherein said DPPC and said MSPC are contained in a molar ratio from about 99:1 to about 70:30.

104 (Withdrawn and previously presented): The liposome of claim 93, wherein said second component is one or more bile acids.

105-108 (Canceled).

109 (Withdrawn and previously presented): The liposome of claim 93, wherein said second component is one or more ceramides.

110 (Withdrawn and previously presented): The liposome of claim 93, wherein said second component is one or more PEG-ceramides.

111-112 (Canceled).

113 (Withdrawn and previously presented): The liposome of claim 93, wherein said second component is one or more fatty acids.

114 (Withdrawn and previously presented): The liposome of claim 93, wherein said second component is the active agent.

115 (Withdrawn and previously presented): The liposome of claim 114, wherein said active agent is a pharmacologically active agent selected from the group consisting of ceramides and platelet activating factor.

116 (Previously presented): The liposome of claim 93, having a diameter of from about 50 nanometers to about 400 nanometers.

117 (Previously presented): The liposome of claim 93, wherein said one or more phospholipids have two acyl chains each comprising 16 to 24 carbon atoms.

118 (Previously presented): The liposome of claim 93, wherein said one or more phospholipids have two acyl chains each comprising 18 to 22 carbon atoms.

119 (Previously presented): The liposome of claim 93, wherein said gel-phase lipid

bilayer further comprises a phospholipid derivatized with a hydrophilic polymer.

120 (Previously presented): The liposome of claim 119, wherein said hydrophilic polymer is selected from the group consisting of polyethylene glycol, polylactic acid, polyglycolic acid, copolymers of polylactic acid and polyglycolic acid, polyvinyl alcohols, polyvinylpyrrolidone; oligosaccharides, and mixtures thereof

121 (Previously presented): The liposome of claim 93, wherein said active agent is a pharmacologically active agent selected from the group consisting of anesthetics, antihistamines, antineoplastics, anti-ulceratives, anti-seizure agents, muscle relaxants, immunosuppressive agents, anti-infective agents, non-steroidal anti-inflammatory agents, imaging agents, nutritional agents, and mixtures thereof.

122 (Previously presented): The liposome of claim 121, wherein said active agent is selected from the group consisting of antineoplastic agents, non-steroidal anti-inflammatory agents, immunosuppressive agents, and anti-infective agents.

123 (Previously presented): The liposome of claim 121, wherein said active agent is an antihistamine.

124 (Currently amended): The liposome of claim 121, wherein said active agent is an antineoplastic agent ~~or an antitumor agent~~.

125 (Previously presented): The liposome of claim 121, wherein said active agent is

selected from the group consisting of methotrexate, doxorubicin, epirubicin, daunorubicin, vincristine, vinblastine, etoposide, ellipticine, camptothecin, paclitaxel, docetaxol, cisplatin, prednisone, methylprednisone, and navalbene.

126 (Previously presented): The liposome of claim 125, wherein said active agent is paclitaxel.

127 (Previously presented): The liposome of claim 125, wherein said active agent is camptothecin.

128 (Previously presented): The liposome of claim 125, wherein said active agent is doxorubicin.

129 (Previously presented): The liposome of claim 125, wherein said active agent is a non-steroidal anti-inflammatory agent.

130 (Previously presented): The liposome of claim 129, wherein said active agent is ibuprofen.

131 (Previously presented): The liposome of claim 93, wherein said active agent is within the liposome interior.

132 (Previously presented): The liposome of claim 93, wherein the acyl groups of the

phospholipid are saturated.

133 (Previously presented): The liposome of claim 93, wherein said phospholipid and said second component are contained in a molar ratio of from about 99:1 to about 51:49.

134 (Previously presented): The liposome of claim 133, wherein said phospholipid and said second component are contained in a molar ration of from about 99:1 to about 70:30.

135 (Previously presented): The liposome of claim 134, wherein said second component is one or more lysolipids.

136 (Previously presented): The liposome of claim 93, wherein said active agent is within the liposome interior and in the gel-phase lipid bilayer membrane.

137 (Previously presented): A method of administering an active agent to a preselected target site in a subject's body, comprising:

(a) administering a liposome to the subject, wherein the liposome comprises:
a gel-phase lipid bilayer membrane having a phase transition region having an onset temperature, a peak transition temperature and an end point temperature;
a liposome interior defined by the gel-phase bilayer;
and an active agent,

wherein the gel-phase lipid bilayer membrane comprises:

(i) a first component which is one or more phospholipids selected from the group consisting of phosphatidyl cholines, phosphatidyl glycerols. phosphatidyl inositols,

phosphatidyl ethanolamines, and sphingomyelins, wherein the one or more phospholipids have two acyl groups; and

(ii) a second component selected from:

(I) one or more surface active agents selected from the group consisting of dichain phospholipids, lysolipids, bile acids, myristoyl surfactants, palmitoyl surfactants, stearoyl sürfactants, ceramides, PEG-ceramides, PEG-phospholipids, C18-ether linked lysophosphatidyl choline, block copoiymers, fatty acids, and mixtures thereof; or

(II) the active agent, wherein the active agent is selected from the group consisting of a pharmacologically active agent, a flavor agent, or a diagnostic agent, or a nutritional agent; and,

(iii) wherein the active agent, if absent from the gel-phase lipid bilayer membrane is present in the liposome interior; and

(iv) wherein the amount of the second component in the gel-phase lipid bilaycr membrane is sufficient to increase a first percentage of active agent released from the liposomc at the phase transition region, compared to a second percentage of active agent released at the transition region of a liposome comprising only the first component; and

(b) heating the subject's preselected target site to a temperature of about 38°C to 45°C to release the active agent from the liposome at the target site.

138 (Previously presented): The method of claim 137, wherein the preselected target site comprises tumor tissue.

139 (Previously presented): The method of claim 137, wherein the liposome comprises an antineoplastic agent.

140 (Previously presented): The method of claim 139, wherein the antineoplastic agent is

selected from the group consisting of methotrexate, doxorubicin, epirubicin, daunorubicin, vincristine, vinblastine, ctoposide, ellipticine, camptothecin, paclitaxel, docetaxol, cisplatin, prednisone, methyl-prednisone, and navalbene.

141 (Previously presented): The method of claim 137, wherein said administration in (a) comprises intravenous administration.

142 (Previously presented): The method of claim 137, wherein the acyl groups of the phospholipid are saturated.

143 (Previously presented): The method of claim 137, wherein the liposome comprises from about 1 to about 50 mole percent of the second component.

144 (Previously presented): The method of claim 143, wherein the liposome comprises from about 1 to about 30 mole percent of the second component.

145 (Previously presented): The method of claim 137, wherein the second component is one or more lysolipids.

146 (Previously presented): The method of claim 145, wherein the lysolipids are selected from the group consisting of monopalmitoylphosphatidylcholine (MPPC), monolaurylphosphatidylcholine (MLPC), monomyristoylphosphatidylcholine (MMPC), monostearoylphosphatidylcholine (MSPC), and mixtures thereof

147 (Previously presented): The method of claim 137, wherein the active agent is entrapped within the interior of the liposome.

148 (Previously presented): The method of claim 137, wherein the active agent is entrapped within the gel-phase lipid bilayer membrane of the liposome.

149 (Previously presented): The method of claim 137, wherein the liposome has a diameter of from about 50 nanometers to about 400 nanometers.

150 (Previously presented): The method of claim 137, wherein the gel-phase lipid bilayer membrane further comprises a phospholipid derivatized with a hydrophilic polymer.

151 (Previously presented): The method of claim 150, wherein the hydrophilic polymer is selected from the group consisting of polyethylene glycol, polylactic acid, polyglycolic acid, copolymers of polylactic acid and polyglycolic acid, polyvinyl alcohols, polyvinylpyrrolidone, oligosaccharides, and mixtures thereof.

152 (Previously presented): The method of claim 137, wherein the active agent is a pharmacologically active agent selected from the group consisting of anesthetics, antihistamines, antineoplastics; anti-ulceratives, anti-seizure agents, muscle relaxants, immunosuppressive agents, anti-infective agents, non-steroidal anti-inflammatory agents, imaging agents, nutritional agents, and mixtures thereof

153 (Previously presented): The method of claim 152, wherein the active agent is selected from the group consisting of antineoplastic agents, non-steroidal anti-inflammatory agents, immunosuppressive agents, and anti-infective agents.

154 (Previously presented): The method of claim 152, wherein the active agent is an antihistamine.

155 (Previously presented): The method of claim 152, wherein the active agent is a non-steroidal anti-inflammatory agent.

156 (Previously presented): The method of claim 155, wherein the active agent is ibuprofen.

157 (Withdrawn and previously presented): The method of claim 137, wherein the second component is the active agent.

158 (Withdrawn and previously presented): The method of claim 157, wherein the active agent is selected from the group consisting of apoptopic agents and platelet activating factor.

159 (Previously presented): The method of claim 137, wherein the active agent is within the liposome interior and in the gel-phase lipid bilayer membrane.

160 (Previously presented): The method of claim 146, wherein the lysolipid is

monostearoylphosphatidylcholine (MSPC).

161 (Previously presented): The method of claim 159, wherein the phospholipid is dipalmitoylphosphatidycholine (DPPC).

162 (Previously presented): The liposome of claim 93, wherein said phase transition region has an onset temperature of about 38°C.

163 (Previously presented): The liposome of claim 93, wherein said phase transition region has a peak transition temperature of about 38°C to about 45°C.

164 (Previously presented): The method of claim 137, wherein said phase transition region has an onset temperature of about 38°C.

165 (Previously presented): The liposome of claim 137, wherein said phase transition region has a peak transition temperature of about 38°C to about 45°C.

166 (Previously presented): A pharmaceutical composition comprising a pharmaceutically acceptable diluent or carrier and one or more liposomes of claim 93.

167 (Previously presented): The pharmaceutical composition of claim 166, wherein the liposomes are dispersed in an aqueous solution.

168 (Previously presented): The pharmaceutical composition of claim 167, comprising physiological saline or phosphate buffered physiological saline.

169 (Previously presented): A pharmaceutical composition comprising a pharmaceutically acceptable diluent or carrier and one or more liposomes of any one of claims 94-136.

170-175 (Canceled).

176 (New) A liposome having a gel-phase bilayer membrane, comprising:

an active agent selected from the group consisting of a pharmacologically active agent, a therapeutic agent, a flavor agent, a diagnostic or imaging agent, a nutritional agent, and combinations thereof,

wherein the gel-phase bilayer has a phase transition temperature of 39 to 45°C, and wherein the gel-phase lipid bilayer membrane comprises:

(a) a first component which is dipalmitoylphosphatidylcholine (DPPC) in an amount ranging from 80 to 98 mol %; and

(b) a second component selected from the group consisting of monostearoylphosphatidylcholine (MSPC) and monopalmitoylphosphatidylcholine (MPPC) in an amount ranging from 2 to 20 mol%.

177 (New): The liposome of claim 176, wherein said active agent is selected from the group consisting of methotrexate, doxorubicin, epirubicin, daunorubicin, vincristine, vinblastine, etoposide, ellipticine, camptothecin, paclitaxel, docetaxol, cisplatin, prednisone, methyl-prednisone, and navalbene.

178 (New): The liposome of claim 177, wherein said active agent is paclitaxel.

179 (New): The liposome of claim 177, wherein said active agent is camptothecin.

180 (New): The liposome of claim 177, wherein said active agent is doxorubicin.

181 (New): The liposome of claim 176, wherein said active agent is a non-steroidal anti-inflammatory agent.

182 (New): The liposome of claim 181, wherein said active agent is ibuprofen.

183 (New): A liposome having a gel-phase bilayer membrane, comprising:

an active agent selected from the group consisting of a pharmacologically active agent, a therapeutic agent, a flavor agent, a diagnostic or imaging agent, a nutritional agent, and combinations thereof,

wherein the gel-phase bilayer has a phase transition temperature of 39 to 45°C, and wherein the gel-phase lipid bilayer membrane comprises:

(a) a first component which is dipalmitoylphosphatidylcholine (DPPC) in an amount ranging from 80 to 98 mol %; and

(b) a second component selected from the group consisting of:

(i) monostearoylphosphatidylcholine (MSPC) and 1,2-distearoyl-sn-glycero-3-phosphoethanolamine-N-[poly(ethyleneglycol) 2000] (DSPE-PEG-2000) in an amount ranging from 2 to 20 mol%; and

(ii) monopalmitoylphosphatidylcholine (MPPC) and 1,2-distearoyl-sn-glycero-3-phosphoethanolamine-N-[poly(ethyleneglycol) 2000] (DSPE-PEG-2000) in an amount ranging from 2 to 20 mol%.

184 (New): The liposome of claim 183, wherein said active agent is selected from the group consisting of methotrexate, doxorubicin, epirubicin, daunorubicin, vincristine, vinblastine, etoposide, ellipticine, camptothecin, paclitaxel, docetaxol, cisplatin, prednisone, methyl-prednisone, and navalbene.

185 (New): The liposome of claim 184, wherein said active agent is paclitaxel.

186 (New): The liposome of claim 184, wherein said active agent is camptothecin.

187 (New): The liposome of claim 184, wherein said active agent is doxorubicin.

188 (New): The liposome of claim 183, wherein said active agent is a non-steroidal anti-inflammatory agent.

189 (New): The liposome of claim 188, wherein said active agent is ibuprofen.